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EXAMINER	
SCHUBERG, LAURA J	

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1657	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/524,231	GRIFFITH, MAY	
	Examiner	Art Unit	
	LAURA SCHUBERG	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *12-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/23/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-27 are pending. Claim 27 has been added, claims 1 and 2 have been amended and no claims have been canceled.

Claims 12-26 were withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 3/5/2007.

Claims 1-11 and 27 have been examined on the merits.

Response to Arguments

Applicant's arguments filed 02/07/2008 have been fully considered but they are not persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Applicant argues that since the newly amended claims require that the claimed composition be formed *in vitro*, that the Jacob reference does not anticipate independent claim 1.

This is not found persuasive because claim 1 is a product-by-process claim. M.P.E.P. § 2113 reads, "Product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps."

"Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of

a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted).

The structure implied by the process steps should be considered when assessing the patentability of product-by-process claims over the prior art, especially where the product can only be defined by the process steps by which the product is made, or where the manufacturing process steps would be expected to impart distinctive structural characteristics to the final product. See, e.g., *In re Garnero*, 412 F.2d 276, 279, 162 USPQ 221, 223 (CCPA 1979)

The use of 35 U.S.C. §§ 102 and 103 rejections for product-by-process claims has been approved by the courts. "[T]he lack of physical description in a product-by-process claim makes determination of the patentability of the claim more difficult, since in spite of the fact that the claim may recite only process limitations, it is the patentability of the product claimed and not of the recited process steps which must be established. We are therefore of the opinion that when the prior art discloses a product which reasonably appears to be either identical with or only slightly different than a product claimed in a product-by-process claim, a rejection based alternatively on either section 102 or section 103 of the statute is eminently fair and acceptable. As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972).

Therefore, since the composition of Jacob meets all the structural limitations of Applicant's claimed invention, the composition of Jacob is deemed to anticipate the invention as claimed.

Applicant argues that since the newly amended claims require that the biopolymer be a "naturally occurring polymer" that the teaching of Simpson can not render claim 1 obvious as Simpson requires electroprocessed collagen. Applicant asserts that electroprocessed collagen is not naturally occurring and that Simpson teaches away from the present invention, which makes use of naturally occurring (non-electroprocessed) biopolymers.

This is not found persuasive because Applicant's disclosure clearly indicates that the naturally occurring polymer may be processed and still be considered a biopolymer (page 16 lines 14-29). Applicant states on page 16 that the collagen can be denatured or derivatised in order to render the collagen useful for the claimed invention. Clearly a collagen that has been modified is still considered to be a biopolymer in light of Applicant's specification. In addition, those of skill in the art of tissue engineering with collagen consider processed collagen to be a biopolymer as well. Dai et al teach that "there is a long history of the use of biopolymer matrices made from processed human or animal tissues" (US 6,696,074, column 1 lines 55-56). In addition, Simpson teaches that naturally occurring organic materials include any substances naturally found in the body of plants or other organisms, regardless of whether those materials have or can be produced or altered synthetically (page 4 para 47).Clearly Simpson does not teach away from a biopolymer that is naturally occurring.

Therefore, the processed collagen of Simpson is deemed to meet the claimed limitation of biopolymer that is naturally occurring in light of Applicant's specification, Simpson's disclosure and those of ordinary skill in the art of tissue engineering.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 3, 7-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Jacob et al (US 2002/0007217 A1).

Amended claim 1 is drawn to an innervated artificial tissue comprising: a) a bio-synthetic matrix comprising a synthetic polymer and a biopolymer; b) a plurality of non-nerve cells associated with the matrix; and c) a plurality of functional nerve cells associated with the matrix; wherein the synthetic polymer comprises one or more N-alkyl or N,N-dialkyl substituted acrylamide co-monomer, one or more hydrophilic co-monomer, **OR** one or more acryl- or methacrylcarboxylic acid co-monomer derivatised to contain a pendent crosslinkable moiety, or combination thereof and wherein the tissue is formed in vitro and wherein the biopolymer is a naturally-occurring polymer.

Dependent claims include specific polymers, the capability of the non-nerve cells of growing as confluent layers over or in the matrix, the addition of bioactive agents, and wherein the artificial tissue is formed as an artificial cornea.

Jacob teaches a synthetic device for cornea replacement that includes corneal enhancement molecules, specifically, extracellular matrix proteins, corneal growth factors, and other ligand-specific enhancer molecules on the surface of an optical polymer wherein the epithelial cell response can be significantly enhanced (page 6 para 45). The optical polymer includes collagen, poly(2-hydroxyethylmethacrylate), polymethacrylic acid or combinations thereof (page 6 para 46). Examples of ligand-specific corneal enhancers include the neurotransmitter, substance P, and fibronectin adhesion-promoting peptide sequences consisting of YIGSR (page 7 para 48). Jacob also teaches that the cornea is heavily innervated with sensory nerve fibers and that this innervation plays an important role in the maintenance of the normal structure and functions of the cornea and in the wound healing process (page 2 para 12). Therefore, with the inclusion of substance P and YIGSR, the implantation of the artificial cornea of Jacob would inherently include cellular ingrowth into the synthetic device that would include both nerve and non-nerve cells. These cells are also inherently capable of growing as confluent layers over or in the matrix.

Since Applicant's invention as claimed does not require that the innervated artificial tissue be formed *in vitro*, the teaching of Jacob anticipates Applicant's invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-3, 7-9, 11 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Simpson et al (US 2002/0090725 A1).

Simpson teaches the formation of an engineered tissue using collagen, as an extracellular matrix, with cells and synthetic matrix materials that include poly(acrylic acid) and other similar synthetic polymers (page 4 para 63). Combinations of different types of cells can be used (page 5 para 66) and can be deposited within or on the matrices (page 5 para 65). The types of cells include neurons (nerve cells) and non-nerve cells (page 8 para 92-page 9 para 92). Addition of bioactive factors is included as well (page 9 para 97-98). The ability to use the matrices to bioengineer tissue or organs

is suggested and corneas are listed as examples of bioengineered components (page 24 para 204). Nerve growth factor is taught as an optional additive to cause innervation of the tissue matrix after implantation (page 25 para 207). Using cells that are capable of growing as a confluent layer over the matrix is also suggested (page 35 example 15 and page 38 example 24). Derivatives of the biopolymer are taught as well (page 4 para 49). Simpson teaches that naturally occurring organic materials include any substances naturally found in the body of plants or other organisms, regardless of whether those materials have or can be produced or altered synthetically (page 4 para 47).

While Simpson does not combine all the limitations taught into a single embodiment, the claimed invention as a whole was prima facie obvious since all the claimed limitations are taught and suggested by the reference.

One of ordinary skill in the art would have been motivated and had a reasonable expectation of success in making these combinations to form the innervated artificial tissue as claimed by Applicant because they are taught and suggested by the reference as reasonable additives to the composition.

Therefore, the teaching of Simpson renders obvious Applicant's invention as claimed.

Claims 4-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Simpson et al (US 2002/0090725 A1) as applied to claims 1-3, 7-9 and 11 and 27 above, and further in view of Chaouk et al (US 6,225,367 B1), Moussy et al (US 6,497,729 B1) and Clapper et al (US 6,514,734 B1).

Simpson suggests an innervated artificial tissue as described above, but does not specifically include wherein the synthetic polymers comprise the specific polymer combinations of claims 4, 5, and 6. However, Simpson specifically teaches that many other synthetic polymers that may be developed are biologically compatible and include copolymers and blends and any other combinations of listed polymers (such as poly(acrylic acid)) with other polymers generally. The use of the polymers will depend on given applications and specifications required (page 5 para 63).

Chaouk teaches biocompatible polymers and products formed therefrom, including optical devices and implants (column 1 lines 1-5). N,N dimethyacrylamide is listed as a suitable polymer that is preferred (column 13 lines 1-9). The polymers of the invention are highly biocompatible with living tissue and support the attachment and growth of human or animal cells *in vivo* or *in vitro* (column 19 lines 47-50). The polymers of the invention are therefore particularly useful as medical implants such as corneal implants (column 19 line 56- column 20 line 2).

Moussy teaches a tissue/implant interface, comprising an implant and a bioactive polymer and indicates that N,N dimethyacrylamide, N-isopropylacrylamide and combinations thereof are suitable polymers that are preferred (column 5 lines 61-66). Acrylic acid is also taught as a suitable polymer (column 6 line 7). Exemplary implantation sites include, but are not limited to, the eye (column 12 line 3). Exemplary implants include, but are not limited to intraocular lenses, nerve regeneration channels, and corneal bandages (column 12 lines 5-15).

Clapper teaches bioactive polymers that are used to modify the surfaces of existing biomaterials or to generate new biomaterials. Biomedical devices that contain the resultant biomaterials are used for a variety of in vitro and in vivo applications such as cornea lenses (column 11 lines 29-38). Suitable polymers are indicated as acrylic acid (column 4 line 63) and N-acryloxysuccinimide (column 19 line 28).

Therefore, one of ordinary skill in the art would have been motivated to use N,N dimethyacrylamide, N-acryloxysuccinimide, N-isopropylacrylamide, and acrylic acid in the method of Simpson because Simpson teaches that many other synthetic polymers may be developed that are biologically compatible and include copolymers and blends and any other combinations of listed polymers with other polymers generally and Chaouk, Moussy, and Clapper teach that these synthetic polymers are suitable for applications involving corneal implants. One of ordinary skill in the art would have had a reasonable expectation of success because Simpson, Chaouk, Moussy, and Clapper all include applications of suitable polymers for corneal implants and Simpson teaches that the use of the polymers will depend on given applications and specifications required (page 5 para 63).

Therefore, the combined teachings of Simpson, Chaouk, Moussy, and Clapper render obvious Applicant's invention as claimed.

Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Simpson et al (US 2002/0090725 A1) as applied to claims 1-9 and 11 and 27 above, and further in view of Jacob et al (US 2002/0007217 A1).

Claim 10 includes wherein the bioactive agent is a pentapeptide having the amino acid sequence YIGSR.

Simpson suggests an innervated artificial tissue as described above, but does not specifically include wherein the bioactive agent is a pentapeptide having the amino acid sequence YIGSR. However, Simpson does teach that several desirable sequences can be incorporated into synthetic collagen (such as RGD) and that any sequence that can be incorporated into a collagen molecule may be used (page 7 para 79).

Jacob teaches an innervated artificial tissue as described above. Jacob also includes short peptide sequences, such as YIGSR and RGD, that are responsible for cell-surface adhesion binding activity in extracellular adhesion proteins to be chemically incorporated onto polymer surfaces (page 5 para 30). Jacob teaches that these minimal binding sequences have only a fraction of the activity of the entire protein, yet their small size allows then to be incorporated at much higher concentrations than would be possible with entire proteins. The short peptide sequences have the advantage of being relatively stable and their synthetic nature renders them amenable to chemical derivatization and covalent attachment (page 5 para 30).

Therefore, one of ordinary skill in the art would have been motivated to add YIGSR peptide sequences to the innervated artificial tissue of Simpson because Jacob teaches that short peptide sequences, such as YIGSR and RGD, that are responsible

for cell-surface adhesion binding activity in extracellular adhesion proteins can be advantageously incorporated onto polymer surfaces (page 5 para 30). One of ordinary skill in the art would have also been motivated to include YIGSR in the tissue of Simpson because Jacob teaches that YIGSR and RGD have similar properties and functions and Simpson also teaches adding RGD. One of ordinary skill in the art would have had a reasonable expectation of success because Simpson also teaches that any sequence (besides RGD) that can be incorporated into a collagen molecule may be used as well (page 7 para 79).

Therefore, the combined teachings of Simpson and Jacob render obvious Applicant's invention as claimed.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAURA SCHUBERG whose telephone number is (571)272-3347. The examiner can normally be reached on Mon-Fri 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon B Lankford/
Primary Examiner, Art Unit 1651

Laura Schuberg